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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/423,037	02/22/2000	DAVID MICHAEL HEERY	ASZD-P01-228	6259

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EXAMINER	
DUNSTON, JENNIFER ANN	

ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/423,037	HEERY ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-22* is/are pending in the application.

4a) Of the above claim(s) *5,6 and 14-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7,9 and 12* is/are rejected.

7)☒ Claim(s) *3,4,8,10,11 and 13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 October 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to the amendment, filed 2/8/2007. Currently, claims 1 and 3-22 are pending.

Applicant's arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections and objections not reiterated in this action have been withdrawn. **This action is FINAL.**

Election/Restrictions

Applicant elected Group I, LXXLL, SRC-1 and oestrogen receptor species without traverse in the reply filed 11/13/2001.

Claims 14-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/13/2001.

Claims 5-6 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/13/2001.

Currently, claims 1, 3, 4 and 7-13 are under consideration.

Response to Arguments - 35 USC § 112

Applicant's arguments, see pages 2-5, filed 2/8/2007, with respect to the rejection of claims 1, 3, 4 and 7-13 under 35 USC 112, first paragraph, have been fully considered and are persuasive. The previous rejection of claims 1, 3, 4 and 7-13 has been withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 7, 9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al (Nature, Vol. 374, pages 91-94, 1995; see the entire reference) in view of Onate et al (Science, Vol. 270, No. 5240, pages 1354-1357, 1995; see the entire reference). This rejection was made in the Office action mailed 8/6/2006 and is reiterated below.

Lee et al teach that Trip1 interacts with thyroid hormone receptor *in vivo* when the hormone receptor is bound to T_3 ligand (e.g. paragraph bridging pages 91-92; paragraph bridging pages 93-94). The sequence presented at page 93, Figure 2a, indicates that only one B^1XXLL motif is present with in the protein (MXXLL, amino acids 273-277). Lee et al teach placing the fragment of Trip 1 comprising the MXXLL motif in contact with the liganded nuclear thyroid hormone receptor transcription factor and detecting the presence of an interaction in the context of a yeast two-hybrid assay (e.g. paragraph bridging pages 91-92). Lee et al suggest that further analysis of the interaction between Trip1 and thyroid receptor will be required to define the nature of these interactions precisely.

Lee et al do not teach further contacting Trip1 and the liganded thyroid hormone receptor with a potential inhibitor compound.

Onate et al teach the interaction of SRC-1 with liganded progesterone receptor in a yeast two-hybrid assay (e.g. page 1354, left column). Onate et al teach the addition of an NH_2-truncated from of SRC-1 to the interaction of the progesterone receptor and SRC-1 to determine whether it would have an effect on the interaction (e.g. page 1356, left column). Onate et al teach that the ability of the truncated SRC-1 to act as a dominant-negative repressor suggests that it is a genuine coactivator for steroid receptor target gene expression (e.g. page 1356, left column).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of interacting the Trip1 and liganded thyroid receptor of Lee et al to include the use of a truncated from of Trip1 as a potential dominant negative inhibitor of the interaction in the yeast two hybrid assay of Lee et al, as taught by Onate et al for the interaction of SRC-1 and liganded progesterone receptor, because Lee et al and Onate et al teach it is within the ordinary skill in the art to use yeast two hybrid systems to study the interaction of liganded hormone receptors and their protein cofactors.

One would have been motivated to make such a modification in order to receive the expected benefit of being able to better understand the interaction of Trip1 and thyroid receptor as suggested by Lee et al and to determine whether Trip1 is a genuine coactivator for thyroid receptor as taught by Onate et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Arguments - 35 USC § 103

Applicant's arguments filed 2/8/2007 have been fully considered but they are not persuasive.

The response asserts that Lee et al do not teach or suggest that the MXXLL motif is the binding domain or a domain of any significance in the TRIP1 sequence. Further, the response asserts that it would not be deduced from the study of Lee et al that any specific sequence within the 406 TRIP1 amino acid sequence: a) is responsible for liganded nuclear receptor binding or transcriptional regulation; b) is conserved among coactivator proteins, or c) could be used to identify a nuclear receptor inhibitor. This is not found persuasive, because the properties of binding to a liganded nuclear receptor in the process of activating or repressing target genes is an inherent property of the B^1XXLL motif. This motif is present in the TRIP1 fusion proteins that interact with thyroid hormone receptor (Lee et al.; e.g., paragraph bridging pages 91-92; Figure 2A). Lee et al teach five B42-TRIP1 isolates that interact with liganded thyroid hormone receptor (e.g., Figure 2). Each of the isolates contains amino acids 141-406 of TRIP1. Thus, one would conclude that this region is responsible for liganded nuclear receptor binding. The MXXLL motif of TRIP1 is found within amino acids 141-406. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that the first region has a particular level of conservation with other coactivator proteins and that the assay is used to identify a nuclear receptor inhibitor) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The response asserts that the pursuit of homology studies with SRC-1 and known coactivator proteins would be envisaged as an unproductive pathway. This is not found persuasive, because the combination of teachings does not require homology studies. One is only required to use fragments of TRIP1 as an inhibitor of the thyroid hormone receptor-TRIP1 interaction.

The response asserts that there is no motivation to apply the TRIP1 methods to SRC1, and there would be no reasonable expectation of success even if the combination were made. Further, the response asserts that the references teach away from applying the TRIP1 methods to SRC1. This is not found persuasive, because the combination of teachings does not require the application of the TRIP1 methods to SRC1. One is only required to use fragments of TRIP1 as an inhibitor of the thyroid hormone receptor-TRIP1 interaction.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Conclusion

Claims 3, 4, 8, 10, 11 and 13 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claims 3, 4, 7, 8, 10, 11 and 13 are allowable only as they are drawn to the elected species (LXXLL, SRC-1 and oestrogen receptor). The claims must be amended to remove the non-elected subject matter before the claim can actually be allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached at 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

jad

CELINE QIAN, PH.D.
PRIMARY EXAMINER